Effects of Various Medicinal Forms of Progesterone on Lipid Peroxidation and Glutathione Redox System in Skin Tissues of Rats with Experimental Dermatitis

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Activity of glutathione redox system in the dermis and epidermis decreased and the intensity of lipid peroxidation increased in rats with experimental dermatitis. Progesterone normalized these parameters. The most optimal treatment was subcutaneous injections of the hormone in a dose of 7×10^{-9} mol/100g.

Key Words: *skin; dermis; epidermis; allergic dermatitis; hydrocortisone; progesterone; mecigestone; gestogens; glutathione*

Lipid peroxidation (LPO) in rat skin depends on activity of the glutathione redox system regulated by female sex hormones, in particular, progesterone.

Here we studied the effects of various medicinal forms of progesterone on the intensity of LPO and activity of the glutathione redox system in the skin of rats with experimental allergic dermatitis.

MATERIALS AND METHODS

Experiments were performed on adult and young female rats in the diestrus phase [3] weighing 100-180 g. The animals were killed under light ether anesthesia. Skin homogenates were prepared as described elsewhere [7]. The intensity of LPO was estimated by the amplitude of Fe^{2+}-induced slow flash of chemiluminescence [1] and content of thiobarbituric acid reactive substances (TBARS) [6]. Activity of the glutathione redox system was evaluated by the content of reduced glutathione (GSH) and activities of glutathione reductase (GR) and glutathione peroxidase (GPx) measured spectrofluorometrically [2]. Contact allergic dermatitis was induced with nitrochlorobenzene [8]. Progesterone was applied on the skin in 1.5% ointment or subcutaneously injected in a dose of 7×10^{-9} mol/100 g (10^{-5} mol in 1 ml 20% ethanol) for 5 days after the development of dermatitis. Protein concentration was measured by the method of Lowry [9]. The results were analyzed by Student's *t* test.

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RESULTS

The intensity of LPO and parameters of the glutathione redox system in the skin of intact rats were taken as the control. In rats with dermatitis, the content of TBARS increased, especially in the epidermis (Fig. 1), and the activity of glutathione redox system decreased (Fig. 2, *a*, *b*). The content of GSH in the skin decreased 8-fold, in particular in the dermis. Activity of GPx in the epidermis and dermis decreased 1.4- and 3.2-fold, respectively. At the same time, activity of GR in the dermis decreased by 73%, but in the epidermis this parameter increased. Thus, contact dermatitis promoted intensification of LPO against the background of suppressed glutathione redox system. Changes in the glutathione redox system in the dermis were more pronounced than in the epidermis. This fact merits special attention, because the dermis determines topographical peculiarities of epidermis [4].

Progesterone applied in 1.5% ointment for 8 days (prescription used in dermatology) and especially subcutaneously injected to rats with experimental dermatitis alleviated symptoms of inflammation (redness,

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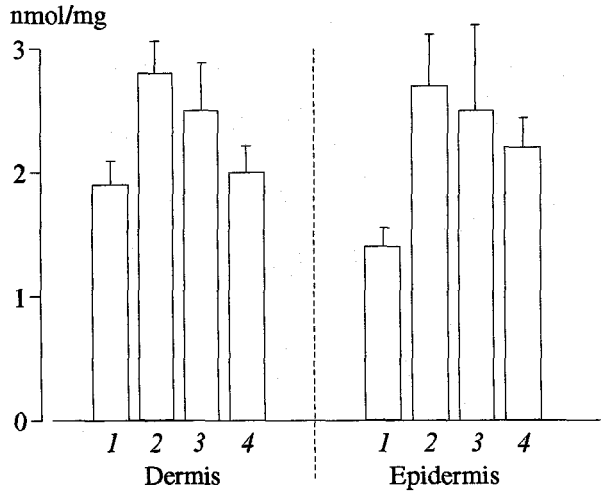

Fig. 1. Content of thiobarbituric acid reactive substances (TBARS) in the skin of rats with experimental allergic dermatitis before and after therapy with progesterone. Ordinate: TBARS content. Here and in Fig. 2: *1*) control; *2*) dermatitis; *3*) dermatitis+1.5% progesterone ointment; and *4*) dermatitis+progesterone (subcutaneous injection).

skin vesicles, and swelling) and 2-fold decreased the size of the inflammatory focus.

Progesterone ointment increased the contents of GSH in the epidermis and dermis by 25 and 10%, respectively, compared with those during dermatitis. Subcutaneous injection of progesterone elevated the contents of GSH in the epidermis and dermis by 48 and 30%, respectively. In the epidermis and dermis, GPx activity increased by 50 and 100%, respectively after the use of progesterone ointment and by 150 and 300%, respectively after subcutaneous injection of this hormone. GR activity in the epidermis increased by 22 and 25%, while in the dermis this parameter was elevated by 3 and 3.5 times under the effect of progesterone applied on the skin and injected subcutaneously, respectively.

Thus, intensification of LPO in the skin accompanying suppression of the antioxidant redox system during experimental allergic dermatitis can be corrected with progesterone applied on the skin and especially subcutaneously injected in a concentration of 10^{-5} M. This is probably related to peculiarities of percutaneous absorption of progesterone. The therapy of allergic skin diseases is directed towards the recovery

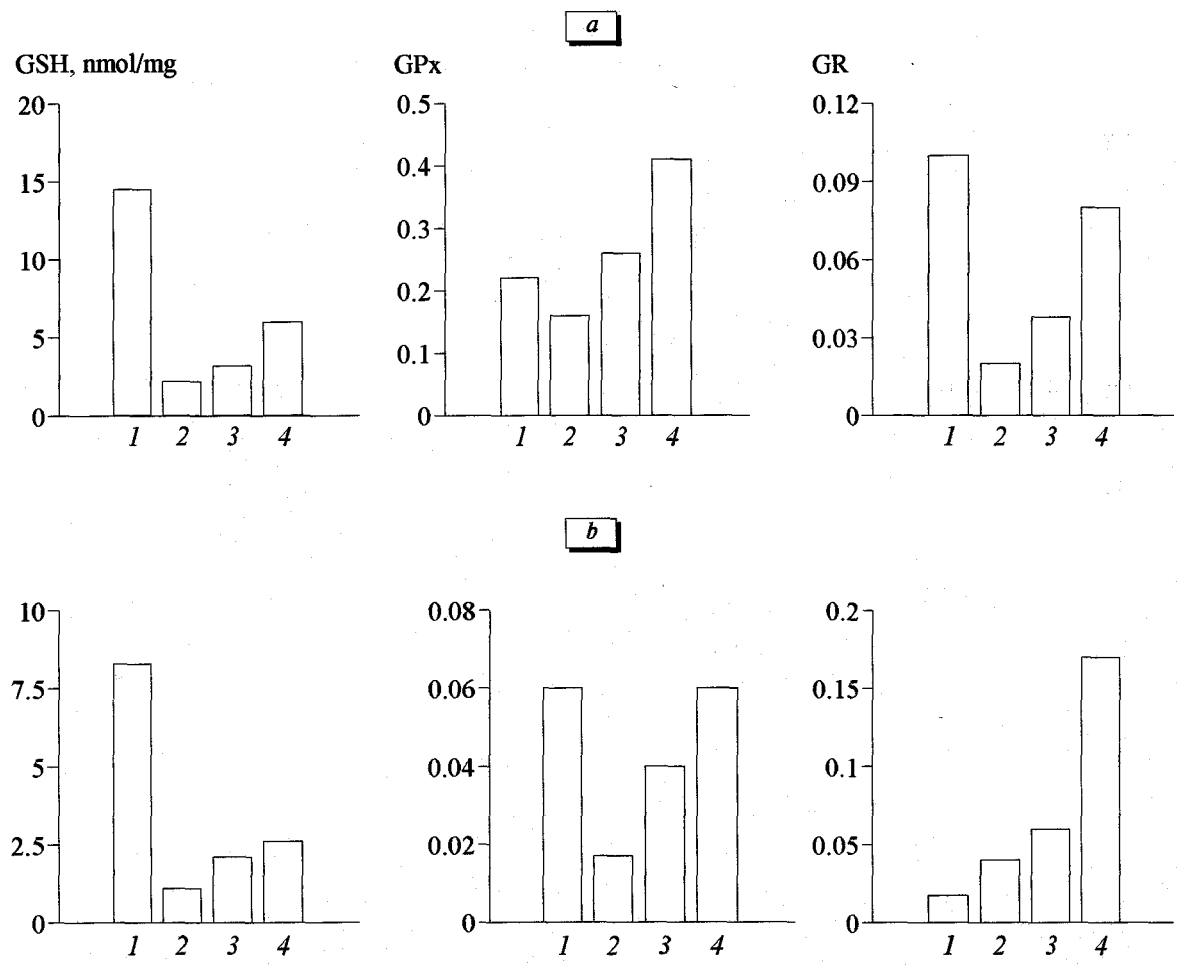

Fig. 2. Activity of glutathione redox system in the epidermis (*a*) and dermis (*b*) of rats with experimental dermatitis. Ordinate: content of reduced glutathione (GSH, nmol/mg) and activities (mmol/mg/min) of glutathione peroxidase (GPx) and glutathione reductase (GR).

of the dermis. Therefore, drugs applied on the skin should be easily absorbed from the surface into deep skin layers and include some additives increasing permeability of skin layers, in particular, of the epidermis.

The comparison of progesterone effects on studied parameters in the skin of intact animals [5] and rats with dermatitis indicates that this drug would be appropriate for therapy of dermatoses associated with disturbances of oxidative and antioxidant systems.

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